



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

APPLICATION NUMBER <b>09/049,865</b>	FILED DATE <b>09/10/00</b>	FIRST NAMED APPLICANT <b>ALBERT WAI-KIT CHAN</b>	ATTY. DOCKET NO. <b>1645 S.M.</b>
---	-------------------------------	---	--------------------------------------

COOPER & DUNHAM  
1185 AVENUE OF THE AMERICANS  
NEW YORK NY 10036

HM22/0710

EXAMINER <b>1645 S.M.</b>
------------------------------

ART UNIT	PAPER NUMBER
----------	--------------

07/13/00

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4/21/00

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s) or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-2, 4-7, 9-17, 20-23, 48-49 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-2, 4-7, 9-17, 20-23, 48-49 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

—SEE OFFICE ACTION ON THE FOLLOWING PAGES—

Art Unit: 1642

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 1-2, 4-7, 9-17, 20-23, 43-47 are being examined.

The following are the remaining rejections.

**REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION**

1. Claims 15-17 are indefinite because claims 15, 16 recite the language "a biologically active substance". It is not clear what kind of activity is referred to.
2. Claims 1-2, 4-7, 9-17, 20-23, 43-47 are rejected under 35 U.S.C. 112, second paragraph, because claim 1 is incomplete, omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: 1) Administration of the cells, and 2) A step correlating back to the preamble.
3. Claims 1-2, 4-7, 9-17, 20-23, 43-47 are indefinite because in claim 1, it is not clear whether the "device" is administered.
4. Claims 10 and 11 are indefinite, because claim 10 does not further limit claim 9, from which claim 10 depends.

Art Unit: 1642

**REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION**

Claims 1-2, 4-7, 9-17, 20-23, 43-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting graft rejection, comprising containing the viable cells or tissues in a device comprising a semipermeable membrane prior to transplantation, and treating a subject transplanted with said cells MR1, or CTLA4, or CTLA4Ig, does not reasonably provide enablement for a method for inhibiting graft rejection, comprising containing the viable cells or tissues in a device comprising a semipermeable membrane prior to transplantation, and treating a subject transplanted with said cells a substance which inhibits an immune system costimulation event. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-2, 4-7, 9-17, 20-23, 43-47 are drawn to a method for inhibiting graft rejection, comprising containing the viable cells or tissues in a device comprising a semipermeable membrane prior to transplantation, and treating a subject transplanted with said cells a substance which inhibits an immune system costimulation event. The specification discloses that a substance, which inhibits an immune system costimulation event, includes, but not limited to, T cell or APC cell surface-molecule analogs (p.27). The specification and the claims encompass a variety of compounds, a substantial number of said compounds would not inhibit an immune system costimulation event.

Art Unit: 1642

It is pointed out that the term "analogs" encompasses a variety of definitions, i.e. chemical modification, deletions, truncations, substitutions, conjugation, etc.. Applicants have not enabled these types of modified T cell or APC cell surface molecules in the specification.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al. *Journal of Cell Biology*, 1990, 11: 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. *Molecular and Cell Biology*, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. *The Journal of Immunology*, 1989, 143(8): 2595-2601, and Gillies et al. *Human Antibodies and Hybridomas*, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

In addition, not any T cell or APC cell surface molecule is involved in interaction between an APC and a T-cell required in conjunction with the binding of an MHC-bound antigen on the surface of the APC to the T cell receptor, e.g. CD2, CD5 or CD7 which are lineage-specific

Art Unit: 1642

markers (Stites, DP et al, eds, 1997, Medical Immunology, Appleton & Lange, Stamford, Connecticut, p.48).

In view of the above unpredictability, and in the absence of a method of how to make a substance which inhibits an immune-response event, one of skill in the art would be forced into undue experimentation in order to perform the claimed invention as broadly as claimed.

### **REJECTION UNDER 35 USC 103**

Rejection under 35 USC 103 of claims 1-2, 4-7, 9-17, 20-23, 43-47 pertaining to obviousness over Lenschow, DJ et al, in view of Goosen et al, Soon-Shiong P et al, Akalin, E et al, Linsley, PS, et al, Padrid PA et al, and Steurer, W et al remains for reasons already of record in paper No. 7.

Applicant argues as follows:

None of the references suggest or teach a combination of containing the viable cells or tissues in a device comprising a semipermeable membrane prior to transplantation, and treating a subject transplanted with said cells a substance which inhibits an immune system costimulation event. There is no suggestion that an increase in prevention of graft rejection would result when combining encapsulation with CTLA4Ig treatment. There is no reasonable expectation that combining Lenschow et al with Goosen et al will result in success. Moreover, the reference by Padrid et al should be removed because said reference discloses CTLA4Ig treatment in an animal model of asthma, and there is no connection between the asthma model and transplantation.

Art Unit: 1642

Furthermore, the statement by the Examiner that "Prevention of graft rejection, but by a different mechanisms, thus by logical reasoning, would increase the chance of preventing graft rejection by the immune system" does not appear to be supported by the combination of teachings of the cited art or by some specific understanding or technological principle within the knowledge of one of ordinary skill in the art.

Applicant's arguments set forth in paper No. 8 have been considered but are not deemed to be persuasive for the following reasons:

In re Kerkhoven (205 USPQ 1069, CCPA 1980) summarizes:

"It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose: idea of combining them flows logically from their having been individually taught in prior art." Neither Lenschow et al. nor Goosen et al. teach a process for inhibiting rejection of transplanted cells by combining encapsulation of transplanted cells with CTLA4Ig treatment. However, in the absence of unexpected results, it would have been prima facie obvious to one of ordinary skill in the art to combine the teachings of the references and to inhibit rejection of transplanted cells by combining CTLA4 Ig treatment and encapsulation of cells used for transplantation. Each of the method of preventing graft rejection had been taught by the prior art.

Applicant asserts that the claimed methods are not obvious in view of the cited references because the cited prior art does not suggest such a combination. However, the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980)

Art Unit: 1642

wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, given the teaching of the prior art of processes inhibiting graft rejection by treating with CTLA4Ig and by encapsulation of cells used for transplantation, it would have been obvious to inhibit graft rejection by using both techniques of graft rejection, i.e. CTLA4Ig treatment and encapsulation of cells to be used in transplantation, because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as methods of inhibiting graft rejection. By logical reasoning, combining two methods of inhibiting graft rejection, each method works by a different mechanism, would increase the chance of preventing graft rejection. One of ordinary skill in the art would have reasonably expected to be successful in inhibiting graft rejection, by combining CTLA4Ig treatment and encapsulation of cells to be used in transplantation, because the methods of CTLA4Ig treatment and encapsulation of cells for use in transplantation have been taught by prior art, and both methods have been successful in inhibiting graft rejection. The citation of Padrid et al is proper, because Padrid et al teach an inherent property of CTLA4Ig treatment, i.e. increasing interferon-gamma.

---

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The

Art Unit: 1642


examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

June 30, 2000

  
SUSAN UNGAR, PH.D  
PRIMARY EXAMINER